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Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 35, 37, 38, 42, 45-48 and 51 are pending in the application. Claims 26-31, 36, 39, 40, 41, 43 and renumbered claims 49 and 50 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein and with reservation to pursue the cancelled subject matter in the future.

Claims 35, 37 and 38 have been amended. Support for the amendments can be found in the specification at least at page 19, lines 16-21, page 20, lines 17-27 and page 39, lines 23-28. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicant(s) respectfully request(s) that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

I. Miscellaneous

Applicants note that the Examiner has renumbered claims 50-52 as claims 49-51.

II. Sequence Compliance

The Examiner has objected to the disclosure as not complying with 37 C.F.R. § 1.821-1.825 and requested that recited sequences in the claims be identified with SEQ ID Nos.

Applicants have amended the claims to insert SEQ ID Nos where deemed appropriate and believe that they are now in compliance with the sequence requirements. Withdrawal of the objections is respectfully requested.

III. Rejection of the Claims Under 35 USC § 112.

A. Claims 35, 39-41, 43 and 45-46.

In the Office Action at page 3, the Examiner rejected claims 35, 39-41, 43, 45 and 46 under 35 U.S.C. § 112, first paragraph. Applicants respectfully traverse this rejection.

Specifically, the Examiner stated that:

> . . . the specification while being enabling for an isolated DNA molecule comprising a DNA sequence encoding the JAK3 kinase amino acid sequence of SEQ ID NO:16 capable of undergoing tyrosine phosphorylation by at least one cytokine or having cytokine receptor binding activity; the same wherein said molecule encodes a JAK3 kinase that is at least 80-99% homologous to the amino acid sequence of SEQ ID NO:16; an expression vector comprising any of said isolated DNA molecule [sic] and an isolated host cell comprising the same expression vector, does not reasonably provide enablement for other embodiments in the claims.

Applicants disagree that "other" embodiments of the claimed invention are not enabled.

In an attempt to support the argument for non-enablement, the Examiner refers to many alleged teachings in the art and states at page 5 of the Office Action that :

> . . . the instant specification is not enabled for the broadly claimed invention for the following reasons. With regard to the breadth of the claims encompassing DNA sequence encoding any and all JAK3 kinase or JAK3 kinase peptide, apart from the disclosure of a mouse cDNA sequence encoding JAK3 kinase of the amino acid sequence of SEQ ID NO:16, the specification fails to teach specifically other cDNA sequences encoding non-mouse Jak3 kinases. For

> examples, the instant specification does not teach the cloning, isolation and characterization of cDNA sequences encoding for human JAK3 kinase of Kawamura et al. (Proc. Natl. Acad. Sci. 91:6374-6378, 1994), Civin et al. (U.S. Patent No. 5,705,625 with the effective filing date of December 15, 1994), Rane & Reddy (Oncogene 9:2415-2423, 1994) or that encoding for rat JAK3 kinase of Takahashi & Shirasawa (FEBS Letters 342:124-128, 1994) and their derived JAK3 kinase peptides.

The Examiner refers to the rejected claims as "encompassing *any and all* JAK3 kinase or JAK3 kinase peptides." This is an incorrect basis for rejecting the claims for at least two reasons. First, Applicants are not claiming "any and all" JAK3 kinase or JAK3 kinase peptides. Rather the claims are drawn to Jak3 kinase peptides that 1) have Jak kinase activity and 2) undergo phosphorylation by at least one cytokine. Further, Applicants have amended claim 35 to add the limitation that the isolated DNA comprise a sequence of SEQ ID NO:16 that encodes at least 400 amino acids of a Jak kinase peptide.

Second, the Examiner appears to base the rejection, at least in part, on the argument that the "specification fails to teach *specifically* other cDNA sequences encoding non-mouse Jak3 kinases." There is no requirement under 35 U.S.C. § 112, first paragraph that requires the specification to "specifically" teach *every* embodiment of a claimed invention. Applicants are merely required to teach one of skill in the art how to make and use the claimed invention without undue experimentation. This, applicants have done.

Merely because others in the art, after the effective filing date of the invention, may have obtained JAK3 kinases whose sequences are not specifically provided in the specification, this does not support an argument for non-enablement. In fact, it supports the opposite position, i.e. that the claimed invention is enabled. The art cited by the Examiner establishes that one of skill in the art would have been capable of obtaining different

embodiments of the invention based either on information present in the application alone or in combination with what such an artisan would have been expected to know as of the application's filing date. Clearly, this establishes that sufficient teachings were available to the skilled artisan to practice the invention without undue experimentation. Merely because certain embodiments may not have been "specifically" taught in the specification, this does not establish lack of enablement.

Various embodiments of the claimed invention are taught in the specification. For example, using the specification either alone or in conjunction with the art there is sufficient guidance for using a Jak kinase cDNA of one species to obtain the corresponding Jak cDNA of another species (see the alignment comparison in Figure 6.) Further evidence of this can be seen in Takahashi *et al.*, *FEBS Letters342*:124-128 (1994) using Jak3 cDNA to detect the Jak3 gene in human, mouse, chicken, snake and frog (*See* page 126, col. 2 of Takahashi). Takahashi, however, while cited by the Examiner is not prior art. (*See* details in rebuttal of the § 102(a) rejection below).

At the bottom of page 3, the Examiner stated that, "the specification fails to teach specifically which JAK3 kinase peptide, which 15 *to* 400 amino acid fragment, which 5 to 335 amino acid fragment." This aspect of the rejection is now moot. The claims reciting these ranges have been cancelled. The Examiner's attention, however, is directed to the fact that amended claim 35 now recites "at least" 400 amino acid limitation. Such a fragment represents a significant portion of the complete sequence and one of skill in the art should have no difficulty in selecting the appropriate portion of the molecule to use in the claimed invention.

The Examiner also stated beginning at page 6, line 6 that the "claims do not even recite any critical elements involved in JAK kinase activity or cytokine receptor binding activity that the encoded JAK kinase peptides need to possess." Applicants fail to understand how recitation of a limitation to require a JAK kinase peptide to undergo tyrosine phosphorylation or have cytokine receptor activity fails to provide a critical element to the claims. In any event, there nothing under 35 U.S.C. § 112, first paragraph requires Applicants to explain how an invention works as the Examiner appears to be requesting by reference to "critical elements" of the invention. It is sufficient to merely provide one of skill in the art with sufficient information to make and use the claimed invention without undue experimentation. This, Applicants have done. Regardless, in an attempt to expedite prosecution, Applicants have further added a size limitation to the amino acid sequence encoded and reference to a specific group of cytokines involved in tyrosine phosphorylation to claim 35. Therefore, this aspect of the rejection is overcome.

The Examiner further stated at page 6, beginning at line 8 of the office action that:

> It is well recognized in the art, any modification (even a "conservative" substitution) to a critical structural region of a protein is likely to significantly alter its functional properties, let alone any extensive deletion or fragmentation or substitution or insertion. The present disclosure offers no guidance as to which regions of the JAK molecule would be tolerant of alteration or fragmentation and which would not, which "particular" amino acid changes at which position and at which combinations, such that the kinase peptides possessing the desired activities as claimed could be obtained. There is a high degree of unpredictability associated with the make [sic] and use of the claimed embodiment. In discussing peptide hormones, Rudinger has stated that "The significance of particular amino acids and sequences for different aspects of biological activity can not be predicted a priori but must be determined from case to case by painstaking experimental study (Page 6, first sentence of Conclusions In J.A. Parsons, ed. "Peptide hormones", University Park Press, 1976). This

> unpredictability is further underscored by the fact that the relationship between the sequence of a peptide and its tertiary structure (or its activity) is not well understood and is not predictable (Ngo et al., In K. Merz et al., ed. "The protein folding problem and tertiary structure prediction", Birkhauser, 1994, 491-495). Moreover, the physiological art is recognized as unpredictable (MPEP 2164.03).

Applicants respectfully disagree. In any event, this aspect of the rejection is now moot since the claims are now limited by recitation to "at least 400 amino acids of a Jak 3 kinase peptide." Based on all of the above, this rejection is overcome and should be withdrawn.

B. Claims 26, 30-31, 35-37, 40, 43 and 45-46

At page 7 of the Office Action, the Examiner rejected claims 26, 30-31, 35-37, 40, 43 and 45-46 under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse this rejection.

The Examiner further argues that "the skilled artisan cannot envision the detailed structure of the broadly claimed isolated DNA molecule comprising a DNA sequence encoding a JAK kinase or a JAK kinase peptide. . ." as well as vectors and host cells containing the claimed DNA. This is now moot because one wishing to practice the invention would know from the amended claim language that the structure of the claimed invention will comprise a DNA sequence encoding at least 400 amino acids found in SEQ. ID. No:16. This clearly allows one of skill in the art to envisage the claimed invention and know that Applicants had possession of the invention as of the filing date. Therefore, based on the amended claim language, this rejection should be withdrawn.

IV. Rejection of Claims 28-29, 31 and 37-41 Under 35 U.S.C. § 112, Second Paragraph

At page 10 of the Office Action, the Examiner rejected claims 28-29, 31 and 37-41 under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants respectfully traverse this rejection.

The rejection, however, is moot as it applies to claims 28-29, 31 and 37. These claims have been cancelled without prejudice or disclaimer.

The Examiner considered claim 38 indefinite because "it is unclear which polypeptides recited in the claim corresponds to which amino acid sequences listed in Figure 6. In addition, the amino acid sequences listed in the claim are not identified by any SEQ ID NO, it is truly confusing." Claim 38 is dependent on claim 35 that now makes reference to SEQ ID NO:16. The addition of SEQ ID No:16 to claim 35 renders moot the rejection.

The Examiner considered claims 39 and 41 unclear because of the recitation" corresponding." This rejection is moot because claims 39 and 41 have been cancelled

In claim 40, the Examiner alleged that the claim was indefinite. Applicants have cancelled this claim. Therefore, the rejection is moot.

Based on all of the above, the rejection of the claims under 35 U.S.C. § 112, second paragraph should be withdrawn.

V. Rejection of the Claims Under 35 U.S.C. § 102(b).

A. Claims 26 and 28

At page 12 of the Office Action, the Examiner rejected claims 26 and 28 under 35

U.S.C. § 102(b) as allegedly being anticipated by Harpur et al. (Oncogene 7:1347-1353, 1992) or Firmbach-Kraft et al. (Oncogene 5:1329-1336, 1990). Applicants respectfully traverse this rejection. Solely in an effort to expedite prosecution, however, and without acquiescing in the propriety of the rejection, Applicants have cancelled claims 26 and 28 without prejudice or disclaimer. Therefore, this rejection is now moot.

B. Claim 26

At page 13 of the Office Action the Examiner rejected claim 26 under 35 U.S.C. § 102 (b) as allegedly anticipated by Wilks et al. (Mol. Cell. Biol. 11: 2057-2065, 1991). Applicants respectfully traverse this rejection. Solely in an effort to expedite prosecution, however, and without acquiescing in the propriety of the rejection, Applicants have cancelled claims 28 without prejudice or disclaimer. Therefore, this rejection is now moot.

VI. Rejection of Claims 26, 28, and 29 Under 35 U.S.C. § 102(e)

In the Office Action at page 13, the Examiner rejected claims 26, 28 and 29 under 35 U.S.C. § 102(e) as being anticipated by Wilks et al. (U.S. Patent No. 5,658,791 with the effective filing date of June 30, 1993). Applicants respectfully traverse this rejection. Solely in an effort to expedite prosecution, however, and without acquiescing in the propriety of the rejection, Applicants have cancelled claims 26, 28 and 29 without prejudice or disclaimer. Therefore, this rejection is now moot.

VII. Rejection of the Claims Under 35 U.S.C. § 102(a)

A. Claims 35, 39-42, 47, 49-51.

In the Office Action at page 14, the Examiner rejected claims 35, 39-42, 47 and 49-51 under 35 U.S.C. § 102(a) as allegedly being anticipated by Kawamura et al. (Proc. Natl. Acad. Sci. 91:6374-6378, 1994 - hereinafter "Kawamura") or Takahashi & Shirasawa (FEBS Letters 342:124-128, 1994 - hereinafter "Takahashi"). Applicants respectfully traverse this rejection.

Solely to expedite prosecution of the application and reserving the right to rebut the rejection on the merits in the future, Applicants submit herewith declarations under 37 C.F.R. § 1.131 from the inventors Drs. Bruce Witthuhn (**Exhibit A**), James Ihle (**Exhibit B**) and Ollie Silvenoinen (**Exhibit C**). Previously, the same set of Exhibits were used for all three inventors and therefore Applicants are submitting only one set of Exhibits with the declarations. The declarations with exhibits were previously submitted in related U.S. Application No:08/665,574 (Now U.S. Patent No: 6,136,595). The declaration addresses embodiments of the inventions related to DNA molecules comprising a DNA sequence encoding an amino acid sequence of a Jak3 kinase peptide and a vector or host comprising said DNA. This Declaration establishes that prior to April 1994, Applicants had in their possession, a full-length clone containing the mJak3 sequence (*See* Paragraph 10 of the Declaration). Additionally, paragraphs 4 and 7 of the declaration provide evidence that Applicants were in possession of partial clones of the Jak kinase molecule.

The undersigned had previously been informed by the publisher of Takahashi that it published between April 1 and April 15, 1994. Further, the undersigned has been informed

by the publisher of Kawamura that it published July 5, 1994. Therefore, based at least on the § 1.131 declaration, Applicants' invention predates both Takahashi. and Kawamura. As such, neither Takahashi nor Kawamura is proper prior art under § 102(a), this rejection of the claims is overcome and should be withdrawn.

B. Claims 43 and 48.

At page 16, the Examiner rejected claims 43 and 48 under 35 U.S.C. 102(a) as allegedly being anticipated by Kawamura or Takahashi. Applicants respectfully traverse this rejection.

As noted above, the cited art was not published before Applicants' invention and is not prior art under 35 U.S.C. § 102(a). Therefore, this rejection is overcome and should be withdrawn.

VIII. Rejection of the Claims Under 35 U.S.C. § 103(a)

A. Claims 26, 30 and 31

At page 18 of the Office Action, the Examiner rejected claims 26, 30 and 31 under 35 U.S.C. 103(a) as allegedly being unpatentable over Harpur et al. (Oncogene 7:1347-1353, 1992) or Wilks et al. (Mol. Cell. Biol. 11:2057-2065, 1991). Applicants respectfully traverse this rejection. The rejection is now moot because Applicants have cancelled the claims without prejudice or disclaimer.

B. Claims 35 and 45-56

At page 19, the Examiner rejected claims 35 and 45-46 under 35 U.S.C. 103(a) as allegedly being unpatentable over Kawamura or Takahashi. Applicants respectfully traverse this rejection.

As indicated above with regard to the § 102(a) rejection, neither Kawamura nor Takahashi is prior art to the claimed invention. Therefore, this rejection is overcome and should be withdrawn.

IX. Rejection of Claims 26, 30, 35-37, 45-47 and 49-51 Obviousness-Type Double Patenting

In the Office Action at page 21, the Examiner rejected claims 26, 30, 35-37, 39-42, 45-47 and 49-51 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,136,595. Applicants respectfully traverse this rejection, however, request that it be held in abeyance until the claims are otherwise in condition for allowance.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicant(s) therefore respectfully request(s) that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicant(s) believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance.

If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (202) 371-2589.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Lawrence B. Bugaisky

Lawrence B. Bugaisky
Attorney for Applicants
Registration No. 35,086

Date: August 28, 2007

1100 New York Avenue, N.W.
Suite 600
Washington, D.C. 20005-3934
(202) 371-2600

Version with markings to show changes made

Substitute the following claim 35 for the pending claim 36.

35. (Once Amended) An isolated DNA molecule comprising a DNA sequence encoding [Jak3 kinase or a] at least 400 amino acids of a Jak3 kinase peptide of SEQ ID NO:16, wherein said peptide has Jak kinase activity and undergoes tyrosine phosphorylation by at least one cytokine selected from the group consisting of IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-9, IL-11, OSM, LIF, G-CSF, EPO, IFN-γ and GM-CSF.

Substitute the following claim 36 for the pending claim 36.

36. (Once Amended) The isolated DNA molecule of [claims 27] claim 35 wherein said molecule encodes a polypeptide having at least one conservative amino acid substitution.

Substitute the following claim 38 for the pending claim 38.

38. (OnceAmended) The isolated DNA molecule of claim 35 comprising a 1500 nucleotide base DNA sequence [encoding a polypeptide selected from the group consisting of amino acids15-1500, 15-1009, 15-1006, 30-600 and 90-1500] of Figure 6 encoding an amino acid sequence of SEQ ID NO: 16.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:
IHLE *et al.*
Appl. No. 08/665,574
Filed: June 18, 1996
For: **Jak Kinases and Regulation of Cytokine Signal Transduction**

Art Unit: 1819
Examiner: Hauda, K.
Atty. Docket: 0656.0370002/SLF/LBB

Declaration of Bruce A. Witthuhn and James N. Ihle Under 37 C.F.R. § 1.131

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

1. We, Bruce Witthuhn and James Ihle state that we are two of the named applicants of the above-captioned application and are co-inventors of the subject matter described and claimed therein.

2. Prior to April 1994, we and Dr. Ollie Silvennoinen reduced to practice in the U.S., the invention of the above-captioned application.

3. Said reduction to practice concerns at least those embodiments of the claimed invention that are related to DNA molecules comprising a DNA sequence encoding an amino acid sequence of a Jak3 kinase peptide and a vector or host comprising said DNA.

4. Prior to April 1994, two clones were obtained that were labeled as B1.1 and B3.1. *In vitro* translation experiments with T3 and T7 primers indicated that clone B3.1 was a partial clone and B1.1 was a full-length clone corresponding in length to other previously identified Jaks. *See* the third lane labeled as B1.1 T_3. **(Exhibit A)**

5. Following additional analysis completed prior to April 1994 it was established that the mJak3 expressed product could be competed out with a specific peptide to Jak3, thereby further supporting the assumption that a full length clone had been obtained. For example, *See* **Exhibit B**.

7. Upon information and belief, prior to April 1994, partial sequencing of subclones from B1.1 was completed by Dr. Silvennoinen. **(Exhibit C)**.

8. Following the partial sequencing of the B1.1 subclones, a full length mJak3 sequence of clone B1.1. was obtained prior to April, 1994. A working copy of this sequence is provided as **Exhibit D**.

9. Upon information and belief, prior to April 1994 a figure containing the complete amino acid sequence encoded by the full-length DNA of mJak3 was prepared by the Biomedical Communications Department at St. Jude. **(Exhibit E).**

10. All of the above results demonstrate that prior to April 1994, a full-length clone containing the mJak3 sequence had been obtained.

11. The attached are true and accurate photocopies (with dates blanked out) of pages taken from the notebooks or other sources of the inventors or those individuals supervised by the inventors.

12. We further state that all statements made are to our knowledge true and that all statements made on information and belief are believed to be true and further that willful false statements and the like are punishable by fine or imprisonment, or both under Section 1001 of Title 18 of the U.S. Code and may jeopardize the validity of the application or any patent issuing thereon.

2/22/99
Date

Bruce A. Witthuhn
Bruce A. Witthuhn

Date

James N. Ihle

P:\USERS\LARRYB\RECENT\656372.dec

1 ul DNA
1 ul Ribosin
2 ul reaction buffer
1 ul polymerase
4 ul ^{35}Trans
25 ul Rabbit Ret Lys
1 ul A. Acid mix
15 ul H_2O

B1.1 B3.1 JAK1 JAK2
T3 : T7 T3 : T7 T3 T3

J1 J2 B1.1 B3.1
T3 T7 T3 T7

IP 5 ul of B1.1 with 10 ul 3015
3029
3030

J2 TK5
TCL 211 1065 3012 TCL 214 1067 3013 TCL 3015 3029 3030

Tube 3013 popped open when boiling - reaction filled with H_2O ~ loaded ± 100 ul on gel of ± 400 ul

Jak1T3
Jak2T3
B1.1T3
B1.1T7
B3.1T3
B3.1T7

In vitro translation

✓1 µl	DNA	JAK1	T_3
✓1 µl	RNasin	JAK2	T_3
✓2 µl	reaction buffer	TK5 B1.1	T_3
✓1 µl	a.a. – M	ERLF from B...	T_7
5 µl	35S trans		
1 µl	Polymerase		
– 14 µl	H_2O		
25 µl	TnT reticulocyte		

Competition

TK5 B1.1 translation

10 µl 3015 + —
10 µl 3015 + 2 µl 10 ng/µl TK5-1
+ 2 µl " TK5-3

10 µl 3029 + —
10 µl 3030 + 2 µl 10 ng/µl TK5 1
5 µl 1067
5 µl 3012

JAK1
211 5 µl
3012 5 µl
1065 5 µl
3015 10 µl

Load gel
HMW TCL 3015P1 + 3029P1
J1 J2 J3 ✓ 3015 ✓ 3015/5.1 3015/5.3 3029 3030

1067 ^ [3012]
mistake J1 B11

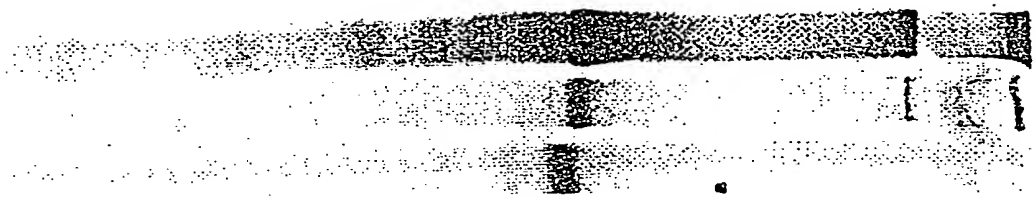
Jak2
214 5 µl
1067 5 µl
3013 5 µl
3015 10 µl

Load gel TCL
HMW 211 3012 1065 3015 J1 J2 J3
214 1067 3013 3015

Fluorograph corresponding to
in vitro translation done by
baw on

Except this lane -
mistakenly loaded as
TK5/3012 IP
actually J1 3012 IP

in vitro translation of DQW



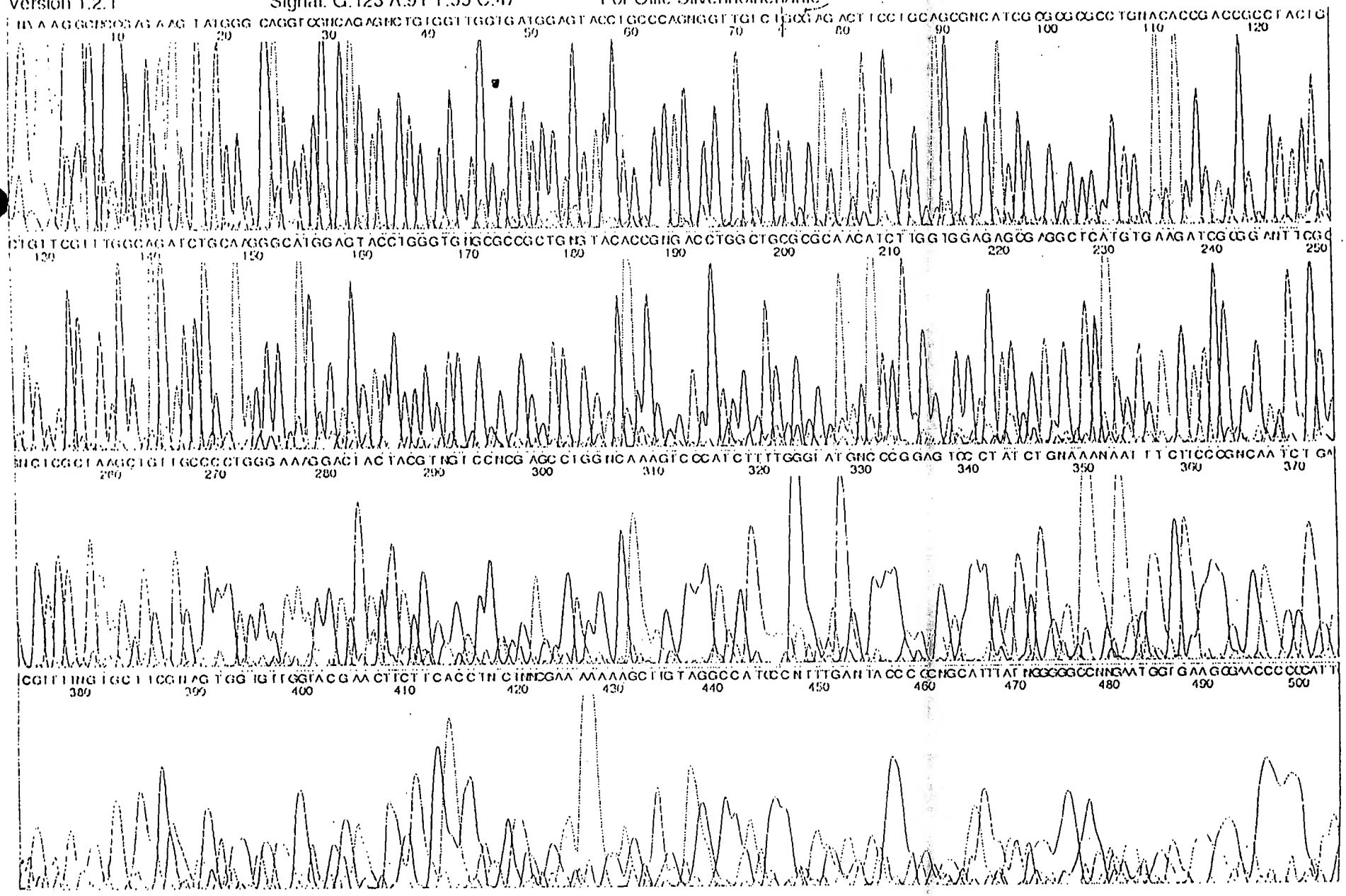
In vitro translation

Applied Biosystems
Model 373A
Version 1.2.1

541os21
DyeTerminator(AnyPrimer)
Lane 21
Signal: G:123 A:91 T:55 C:47

Points 737 to 5937 Base 1: 737
INST FILE 707173
B.1.1+S1b
For Ollie Silvennoinen/Ihle

X: 0 to 6578 Y: 0 to 1200
Spacing: 10.24

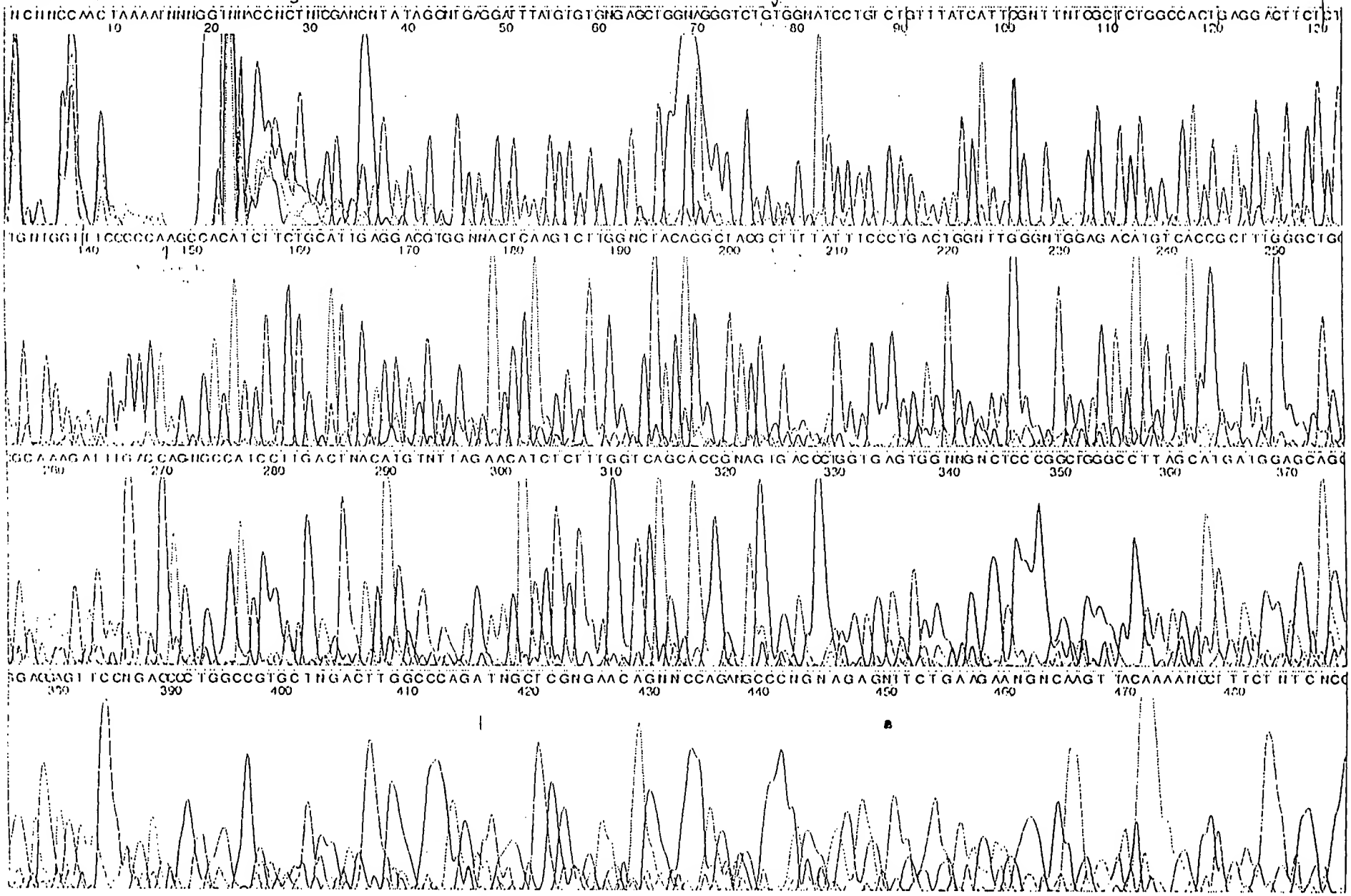


Applied Biosystems
Model 373A
Version 1.2.1

541os22
DyeTerminator(AnyPrimer)
Lane 22
Signal: G:139 A:69 T:59 C:32

Points 631 to 5937 Base 1: 631
INST FILE 707173
B.1.1+S2a
For Ollie Silvennoinen/Ihle

X: 0 to 6897 Y: 0 to 1200
Spacing: 10.00

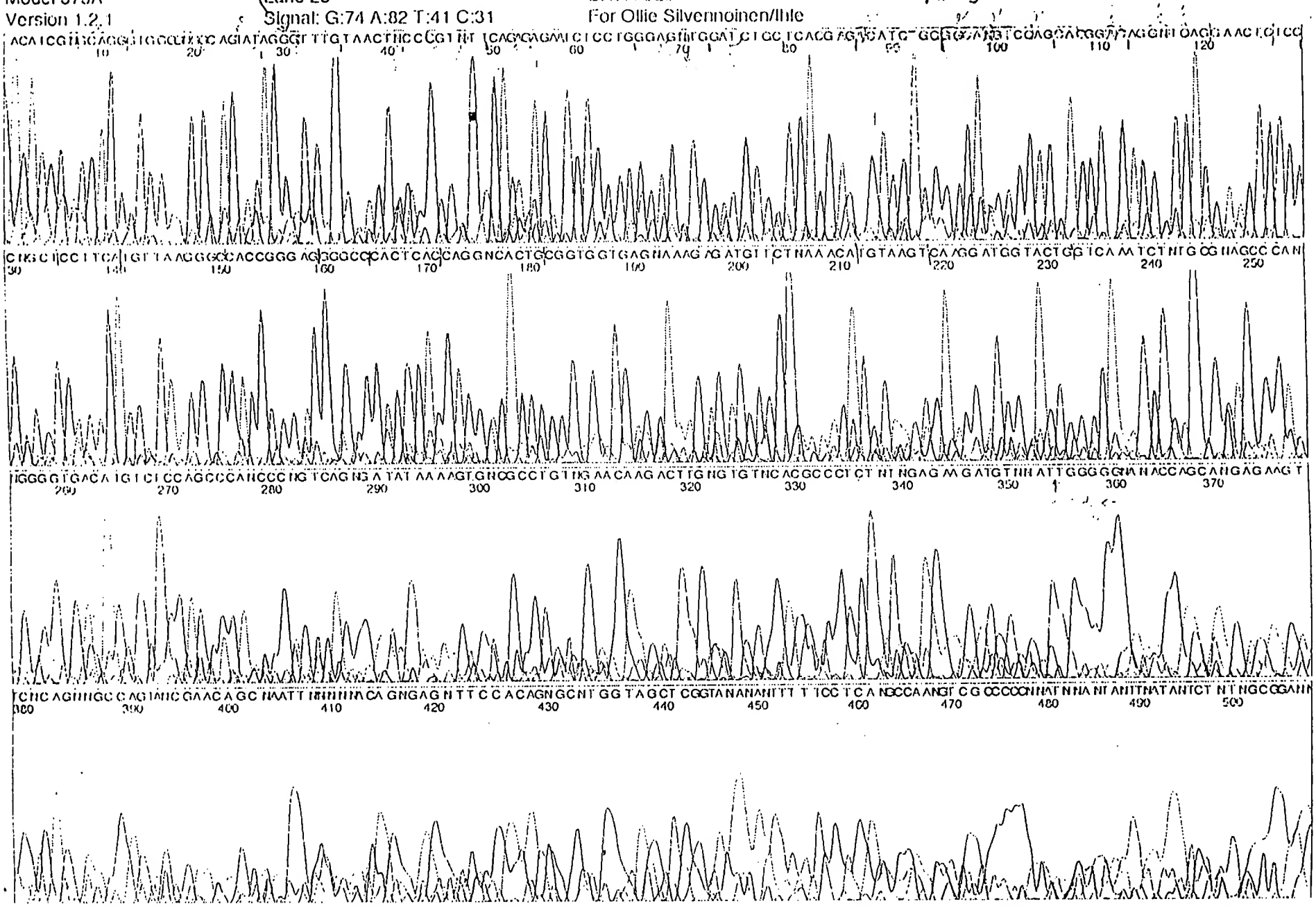


Applied Biosystems
Model 373A
Version 1.2.1

541os23
DyeTerminator(AnyPrimer)
Lane 23
Signal: G:74 A:82 T:41 C:31

Points 931 to 5937 Base 1: 931
INST FILE 707173
B.1.1+S2b
For Ollie Silvermoinen/Ihle

X: 0 to 6190 Y: 0 to 1200
Spacing: 10.41

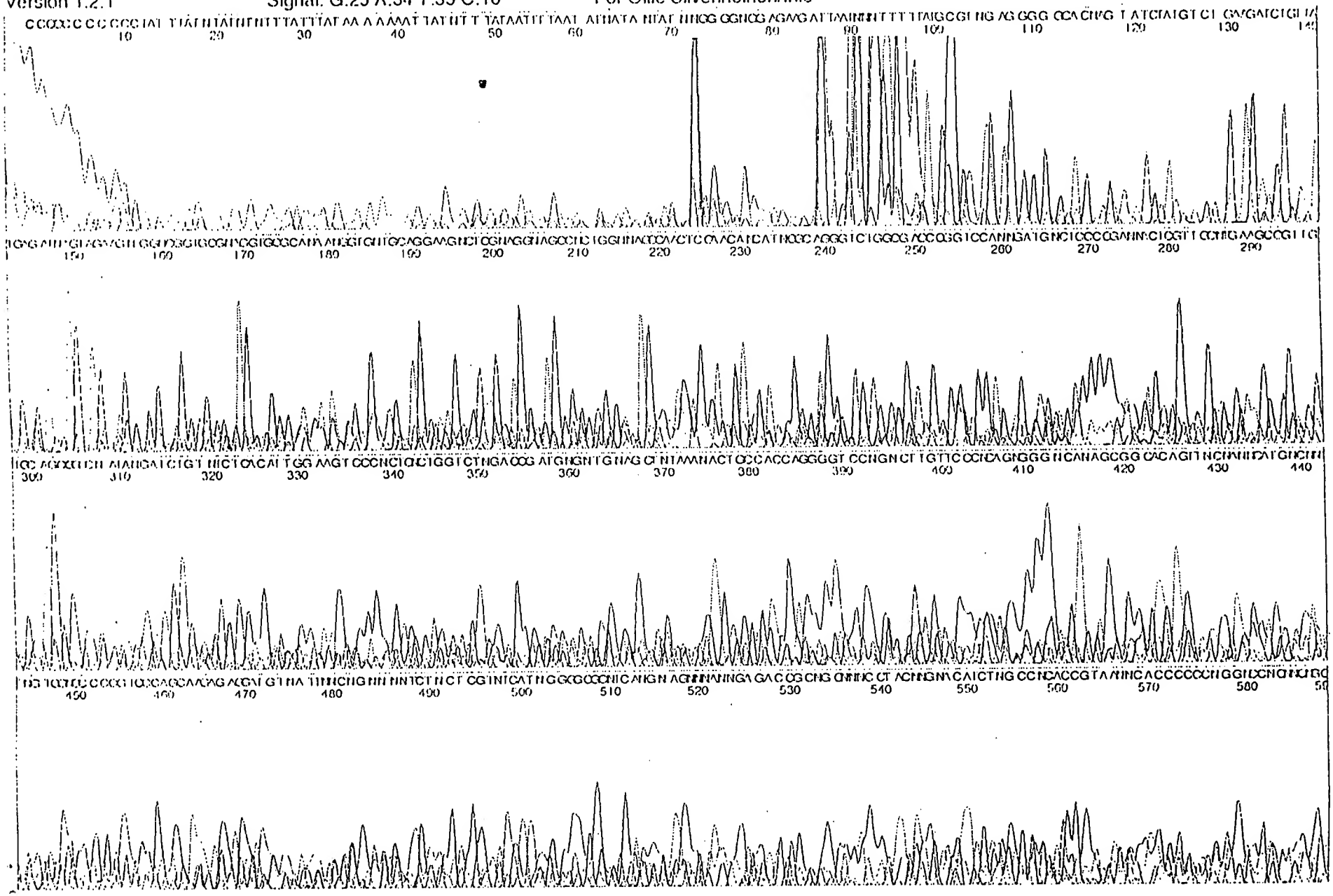


Applied Biosystems
Model 373A
Version 1.2.1

541os20
DyeTerminator(AnyPrimer)
Lane 20
Signal: G:25 A:34 T:35 C:16

Points 0 to 5937 Base 1: 0
INST FILE 707173
B.1.1+S1a
For Ollie Silvennoinen/Ihle

X: 0 to 6347 Y: 0 to 1200
Spacing: -12.00



[redacted] to perform 2 separate searches.
[redacted] searchs of the latest release of GenBank and use
[redacted] OBT BLAST program for homology searchs of newly released sequences.

Use SEARCHNCBI and DBNCBI to search for and retrieve new sequences.

Documentation for the NCBI BLAST and other NCBI programs is in the newsgroup stjude.mbcf. If you need any assistance getting started or using any of the NCBI programs please call the MBCF at ext. 2385 or ext 689.

SEQ:

>>> Closing output file.
>>> At connection #0 (mbcf.stjude.org)

type cc.rec
> O <
O| |O IntelliGenetics
> O <

SEQ - Sequence Analysis System
Version 5.4

SEQ: translate

Default is translation in 3-letter code in one frame.

TRANSLATE: three

TRANSLATE [Three-Frame]: run

Name or number of the sequences to be analyzed (<CR> when done).

Sequence: 3
Sequence:

Would you like the non-coding strand of each sequence to be shown? (<CR>=No)

B1.1E-X

```
                                                    27
ATG GCACCT CCA AGT GAG GAG ACA CCT CTG ATC CCT CAG CGC TCT TGC AGC CTC                54
MET Ala Pro Pro Ser Glu Glu Thr Pro Leu Ile Pro Gln Arg Ser Cys Ser Leu
 Trp His Leu Gln Val Arg Arg His Leu   .  Ser Leu Ser Ala Leu Ala Ala Ser
  Gly Thr Ser Lys   .  Gly Asp Thr Ser Asp Pro Ser Ala Leu Leu Gln Pro Leu

                                                    81
TCA TCT TTA GAG GCA AAA GCC TTG  AT GTG CTC CTT CCT CCC CAG CGA TTG TCA      108
Ser Ser Ser Glu Ala Gly Ala Leu His Val Leu Leu Pro Pro Arg Gly Pro Gly
 His Pro Gln Arg Gln Glu Pro Cys MET Cys Ser Phe Leu Pro Gly Asp Leu Gly
  Ile Leu Arg Gly Arg Ser Leu Ala Cys Ala Pro Ser Ser Pro Gly Thr Trp Ala

                                                   135
TCT CCC CAG CGA TTG TCA TTC TCT TTT GGG GAC TAC TTG GCT GAG GAT TTA TGT      162
Ser Pro Gln Arg Leu Ser Phe Ser Phe Gly Asp Tyr Leu Ala Glu Asp Leu Cys
 Leu Pro Ser Leu Cys His Ser Leu Leu Glu Thr Thr Trp
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Val Ala Ile Val Leu Leu Phe Trp Gly Leu Leu Gly . Gly Phe MET Cys

S2a (217)

189 216

GTC GCA ATT GCC AAG GCA TGT GGG ATC CTG CCT GTT TAT CAT TGG CTT TTC GCT
Val Arg Ala Ala Lys Ala Cys Gly Ile Leu Pro Val Tyr His Ser Leu Phe Ala
Cys Gln Leu Pro Arg Pro Val Gly Ser Cys Leu Phe Ile Ile Arg Phe Ser Leu
Ala Ser Cys Gln Gly Leu Trp Asp Pro Ala Cys Leu Ser Phe Ala Phe Arg Ser

243 270

CTG GCC ACT GAG GAC TTC TGT TGC TGG TTT CCC CCA AGC CAC ATC TTC TGC ATA
Leu Ala Thr Glu Asp Phe Ser Cys Trp Phe Pro Pro Ser His Ile Phe Cys Ile
Trp Pro Leu Arg Thr Ser Leu Ala Gly Phe Pro Gln Ala Thr Ser Ser Ala . .
Gly His . Gly Leu Leu Leu Leu Val Ser Pro Lys Pro His Leu Leu His Arg

297 324

GAG GAC GTG GAC ACT CAA GTC TTG GTC TAC AGG CTA CGC TTT TAT TTC CCT GAC
Glu Asp Val Asp Thr Gln Val Leu Val Tyr Arg Leu Arg Phe Tyr Phe Pro Asp
Arg Thr Trp Thr Leu Lys Ser Trp Ser Thr Gly Tyr Ala Phe Ile Ser Leu Thr
Gly Arg Gly His Ser Ser Leu Gly Leu Gln Ala Thr Leu Leu Phe Pro . Leu

S2b 2nd 349

331 378

TGG TTT GGG CTG GAG ACA TGT CAC CGC TTT GGG CTG CGC AAA GAT TTG ACC AGT
Trp Phe Gly Leu Glu Thr Cys His Arg Phe Gly Leu Arg Lys Asp Leu Thr Ser
Gly Leu Gly Trp Arg His Val Thr Ala Leu Gly Cys Ala Lys Ile . Pro Val
Val Trp Ala Gly Asp MET Ser Pro Leu Trp Ala Ala Gln Arg Phe Asp Gln Cys

S2a ends 2117

405 432

GCC ATC CTT GAC TTA CAT GTT TTA GAA CAT CTC TTT GCT CAG CAC CGC AGT GAC
Ala Ile Leu Asp Leu His Val Leu Glu His Leu Phe Ala Gln His Arg Ser Asp
Pro Ser Leu Thr Tyr MET Phe . Asn Ile Ser Leu Leu Ser Thr Ala Val Thr
His Pro . Leu Thr Cys Phe Arg Thr Ser Leu Cys Ser Ala Pro Gln . Pro

459 486

CTG GTG AGT GGG CGC CTC CCG GTG GGC CTT AGC ATG AAG GAG CAG GGA GAG TTC
Leu Val Ser Gly Arg Leu Pro Val Gly Leu Ser MET Lys Glu Gln Gly Glu Phe
Trp . Val Gly Ala Ser Arg Trp Ala Leu Ala . Arg Ser Arg Glu Ser Ser
Gly Glu Trp Ala Pro Pro Gly Gly Pro . His Glu Gly Ala Gly Arg Val Pro

513 540

CTG AGC CTG GCC GTG CTG GAC TTG GCC CAG ATG GCT CGT GAG GAG GCC CAG CGC
Leu Ser Leu Ala Val Leu Asp Leu Ala Gln MET Ala Arg Glu Glu Ala Gln Arg
. Ala Trp Pro Cys Trp Thr Trp Pro Arg Trp Leu Val Ser Arg Pro Ser Ala
Glu Pro Gly Arg Ala Gly Leu Gly Pro Asp Gly Ser . Ala Gly Pro Ala Pro

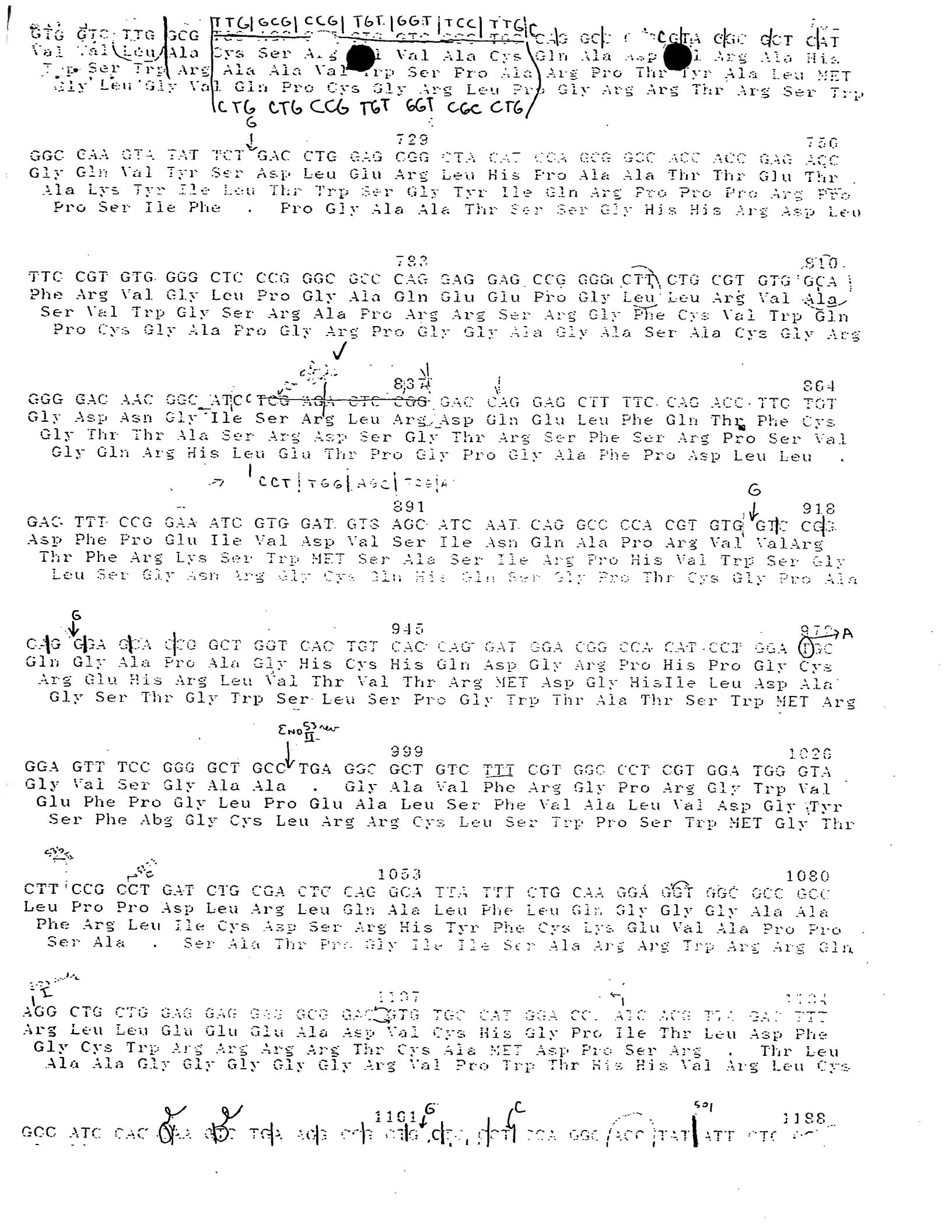
S2b 417 Stop

567 594

CCA GGA GAG CTG CTG AAG ACG GTC AGT TAC AAA GCC TGT CTG CCG CCC AGC CTG
Pro Gly Glu Leu Leu Lys Thr Val Ser Tyr Lys Ala Cys Leu Pro Pro Ser Leu
Gln Glu Ser Cys . Arg Arg Ser Val Thr Lys Pro Val Cys Arg Pro Ala Cys
Arg Arg Ala Ala Glu Asp Gly Gln Leu Gln Ser Leu Ser Ala Ala Gln Pro Ala

621 648

CGC GAT GTG ATC CAG GGC CAG AAC TTC GTG ACA CGC AGG CGC ATC CGC AGG ACC
Arg Asp Val Ile Gln Gly Gln Asn Phe Val Thr Arg Arg Arg Ile Arg Arg Thr
Ala MET . Ser Arg Ala Arg Thr Ser . His Ala Gly Ala Ser Ala Gly Pro
Arg Cys Asp Pro Gly Pro Glu Leu Arg Asp Thr Gln Ala His Pro Gln Asp Arg



... His Pro Pro Ser Leu Lys Ala Ala Ala Pro Ser Arg His Leu Tyr Ser Pro Pro

1215 1242

CGC AGC CCG CAG GAC TAT GAC AGC TTT CTT CTT ACC GCC TGC GTC CAG ACT CCT
Arg Ser Pro Gln Asp Tyr Asp Ser Phe Leu Leu Thr Ala Cys Val Gln Thr Pro
Ala Ala Arg Arg Thr MET Thr Ala Phe Phe Leu Pro Pro Ala Ser Arg Leu Leu
Glu Pro Ala Gly Leu . Glu Leu Ser Ser Tyr Arg Leu Arg Pro Asp Ser Ser

1269 1296

CTT GGC CCC GAC TAC AAG GGC TGC CTC ATC CGC CAG GAC CCA GCG GGG CTT TCT
Leu Gly Pro Asp Tyr Lys Gly Cys Leu Ile Arg Gln Asp Pro Ala Gly Leu Ser
Leu Ala Pro Thr Thr Arg Ala Ala Ser Ser Ala Arg Thr Gln Arg Gly Phe Leu
Trp Pro Arg Leu Gln Gly Leu Pro His Pro Pro Gly Pro Ser Gly Ala Phe Ser

1323 1350

CCC TGG TTG CCT CAG CCA GCC CCA CAG AAG CTG CGG GAG CTG CTT GCA GCC TGC
Pro Trp Leu Pro Gln Pro Ala Pro Gln Lys Leu Arg Glu Leu Leu Ala Ala Cys
Pro Gly Cys Leu Ser Gln Pro His Arg Ser Cys Gly Ser Cys Leu Gln Pro Ala
Leu Val Ala Ser Ala Ser Pro Thr Glu Ala Ala Gly Ala Ala Cys Ser Leu Leu

1377 1404

TGG AAT TCT GGG CTG CGA GTA GAC BGT GCT GCC CTG TAC CTA ACA TCC CGG CGC
Trp Asn Ser Gly Leu Arg Val Asp Gly Ala Ala Leu Tyr Leu Thr Ser Arg Arg
Gly Ile Leu Gly Cys Glu . Thr Val Leu Pro Cys Thr . His Pro Gly Ala
Glu Phe Trp Ala Ala Ser Arg Arg Cys Cys Pro Val Pro Asn Ile Pro Ala Leu

1431 1458

TCC CAG ACC CAA GGA AAA GTC CAA TTG ATC GTG GTG CGA AGG CTG CAC CGC GCC
Ser Gln Thr Gln Gly Lys Val Gln Leu Ile Val Val Arg Arg Leu His Arg Ala
Pro Arg Pro Lys Glu Lys Ser Asn . Ser Trp Cys Glu Gly Cys Thr Ala Pro
Pro Asp Pro Arg Lys Ser Pro Ile Asp Arg Gly Ala Lys Ala Ala Pro Arg Leu

1485 1512

TCC CCG GCT GCT CCC CGT CCT GCT GTG CGC TGA CAC AGC TGA GCT TCC ACA CAA
Ser Pro Ala Ala Pro Arg Pro Ala Val Arg . His Ser . Ala Ser Thr Gln
Pro Arg Leu Leu Pro Val Leu Leu Cys Ala Asp Thr Ala Glu Leu Pro His Asn
Pro Gly Cys Ser Pro Ser Cys Cys Ala Leu Thr Gln Leu Ser Phe His Thr Ile

1539 1566

TTC CAA CGG ACA GCC TGG AGT GGC ACG AGA ACC TGG GTC ACG GTT CTT TTA CCA
Phe Gln Arg Thr Ala Trp Ser Gly Thr Arg Thr Trp Val Thr Val Leu Leu Pro
Ser Asn Gly Gln Pro Gly Val Ala Arg Glu Pro GDy Ser Arg Phe Phe Tyr Gln
Pro Thr Asp Ser Leu Glu Trp His Glu Asn Leu Gly His Gly Ser Phe Thr Lys

1593 1620

AGA TCT TCC GTG GCG CAG GCG GGA GGT CGT GGA TGG TGA GAC ACA TGA CTC GGA
Arg Ser Ser Val Ala Gln Ala Gly Gly Arg Gly Trp . Asp Thr . Leu Gly
Asp Leu Pro Trp Arg Arg Arg Glu Val Val Asp Gly Glu Thr His Asp Ser Glu
Ile Phe Arg Gly Ala Gly Gly Arg Ser Trp MET ValArg His MET Thr Arg Lys

1647 1674

AGT CCT CCT GAA GGT CAT GGA CTC CAG ACA TCA GGAACT GCA TGG AGT CTT TTC
Ser Pro Pro Glu Gly His Gly Leu Gln Thr Ser Gly Thr Ala Trp Ser Leu Phe
Val Leu Leu Lys Val MET Asp Ser Arg His Gln Glu Leu His Gly Val Phe Ser
Ser Ser . Arg Ser Trp Thr Pro Asp Ile Arg Asn Cys MET Glu Ser Phe Leu

1701 1728

TGG AAG CCG CAA GCT TGA [redacted] AAG TAT CCT ACC CGC [redacted] GG TGT TAC TGC
Trp Lys Pro Gln Ala . . [redacted]la Lys Tyr Pro Thr Arg Thr Trp Cys Tyr Cys
Gly Ser Arg Lys Leu Asp Glu Pro Ser Ile Leu Pro Ala Pro Gly Val Thr Ala
Glu Ala Ala Ser Leu MET Ser Gln Val Ser Tyr Pro His Leu Val Leu Leu His

1755 1782

ACG GCG TCT GCA TGG CTG GAG ACA GCA TCA TGG TGC AGG AAT TTG TGT ATC TAG
Thr Ala Ser Ala Trp Leu Glu Thr Ala Ser Trp Cys Arg Asn Leu Cys Ile .
Arg Arg Leu His Gly Trp Arg Gln His His Gly Ala Gly Ile Cys Val Ser Arg
Gly Val Cys MET Ala Gly Asp Ser Ile MET Val Gln Glu Phe Val Tyr Leu Gly

G T
1809 1836

GAG CAA TTG ACA TGT ACC TGC GCA ACG AGG CCA CCT GGT GTC AGC CAG CTG GAA
Glu Gln Leu Thr Cys Thr Cys Ala Thr Arg Pro Pro Gly Val Ser Gln Leu Glu
Ser Asn . His Val Pro Ala Gln Arg Gly His Leu Val Ser Ala Ser Trp Lys
Ala Ile Asp MET Tyr Leu Arg Asn Gly Ala Thr Trp Cys Gln Pro Ala Gly Asn

G
1863 1890

ACT GCA GGT GAC CAA GCA GCT GCA TAT GCC CTT AAC TAC TTG GAG GAC AAA GGC
Thr Ala Gly Asp Gln Ala Ala Ala Tyr Ala Leu Asn Tyr Leu Glu Asp Lys Gly
Leu Gln Val Thr Lys Gln Leu His MET Pro Leu Thr Thr Trp Arg Thr Lys Ala
Cys Arg . Pro Ser Ser Cys Ile Cys Pro . Leu Leu Gly Gly Gln Arg Pro

C
1917 1944

CTT CTC ACG GCA ACG TCT CAG CAC GGA AGG TGC TCC TGG CTC GTG AGG GGG GTG
Leu Leu Thr Ala Thr Ser Gln His Gly Arg Cys Ser Trp Leu Val Arg Gly Val
Phe Ser Arg Gln Arg Leu Ser Thr Glu Gly Ala Pro Gly Ser . Gly Gly .
Ser His Gly Asn Val Ser Ala Arg Lys Val Leu Leu Ala Arg Glu Gly Gly Asp

1971 1998

ATG GGA ATC CAC CTT TCA TTA AGC TGA GTG ATC CTG GTG TCG AGT CCC ACT GTG
MET Gly Ile His Leu Ser Leu Ser . Val Ile Leu Val Ser Ser Pro Thr Val
Trp Glu Ser Thr Phe His . Ala Glu . Ser Trp Cys Arg Val Pro Leu Cys
Gly Asn Pro Pro Phe Ile Lys Leu Ser Asp Pro Gly Val Glu Ser His Cys Ala

Bld 2/2
2025 2052

CTG AGC CTG GAA ATG CTC ACC GAC AGA ATA CCC TGG TGG CCC CCG AAT GTC TCC
Leu Ser Leu Glu MET Leu Thr Asp Arg Ile Pro Trp Trp Pro Pro Asn Val Ser
. Ala Trp Lys Cys Ser Pro Thr Glu Tyr Pro Gly Gly Pro Arg MET Ser Pro
Glu Pro Gly Asn Ala His Arg Gln Asn Thr Leu Val Ala Pro Glu Cys Leu Gln

G A G/G
2079 2106

[illegible] CTC AGA CAC TCT GCT TGG AGG CTG ACA AGT GCC CCT TGG AGC CAC CAC GTG
Lys Leu Arg His Ser Ala Trp Arg Leu Thr Ser Gly Leu Trp Ser His His Val
Ser Ser Asp Thr Leu Leu Gly Gly . Gln Val Gly Phe Gly Ala Thr Thr Trp
Ala Gln Thr Leu Cys Leu Ile Ala Asp Lys Thr [illegible]

2133 2160

GAG [illegible]
Glu Val Phe Thr Gly Thr Arg Pro His His Leu Ala Gly Ala ArgGln Lys Ala
Arg Cys Ser Arg Gly Pro Ala His Ile Thr Ser Leu Glu Pro Ala Lys Lys Leu
Gly Val His Gly Asp Pro Pro Thr Ser Pro Arg Trp Ser Pro Pro Lys Ser .

2187 2214

Lys Phe Tyr Glu Asp Gln Gly Gln Leu Pro Ala Leu Lys Asp Thr Glu Leu Ala
Ser Ser MET Arg Thr Arg Ala Ser Cys Pro Leu Ser Asn Gln Gln Asn Trp Arg

2241 2268
GGG ACT TAT CAC ACA GTG CAT GGC GTA TGA TCC TGG CCG GCG CCC CTC CTT CCG
Gly Thr Tyr His Thr Val His Gly Val . Ser Trp Pro Ala Pro Leu Leu Pro
Gly Leu Ile Thr Gln Cys MET Ala Tyr Asp Pro Gly Arg Arg Pro Ser Phe Arg
Asp Leu Ser His Ser Ala Trp Arg MET Ile Leu Ala Gly Ala Pro Pro Ser Glu

920 Slow Stutter 2/26+3/2

2295 2322
AGC TAT CCT CAG AGA CCT CAA CGG CCT CAT TAC ATC AGA TTA CGA GCT CCC TCA
Ser Tyr Pro Gln Arg Pro Gln Arg Pro His Tyr Ile Arg Leu Arg Ala Pro Ser
Ala Ile Leu Arg Asp Leu Asn Gly Leu Ile Thr Ser Asp Tyr Glu Leu Pro His
Leu Ser Ser Glu Thr Ser Thr Ala Ser Leu His Gln Ile Thr Ser Ser Leu Ile

CTG TCA ← Insert

2349 2376
TTA CAT CAG ATT ACG AGC TCN NNA GAC CCA CAC CTG CAT CCC GAG TCT CGA GAT
Leu His Gln Ile Thr Ser Ser - - Asp Pro His Leu His PrG Glu Ser Arg Asp
Tyr Ile Arg Leu Arg Ala - - Thr His Thr Cys Ile Pro Ser Leu Glu MET
Thr Ser Asp Tyr Glu Leu Leu Ser Arg Pro T'r Pro Ala Ser Arg Val Ser Arg .

2403 2430
GAG CTG TGC GTA GCT GGC GCC CAG CTC TAT GCC TGC CAG GAC CCC GCC ATG ATT
Glu Leu Cys Val Ala Gly Ala Gln Leu Tyr Ala Cys Gln Asp Pro Ala MET Ile
Ser Cys Ala . Leu Ala Pro Ser Ser MET Pro Ala Arg Thr Pro Pro . Phe
Ala Val Arg Ser Trp Arg Pro Ala Leu Cys Leu Pro Gly Pro Arg His Asp Ser

960 ?

2457 2484
CGA GGA GAG ACA CCT TAA GTA CAT CGT CTT TGT CGG GCA AGG GCA ACT TTG GCA
Arg Gly Glu Thr Pro . Val His His Leu Cys Arg Ala Arg Ala Thr Leu Ala
Glu Glu Arg His Leu Lys Tyr Ile Ile Phe Val Gly Gln Gly Gln Leu Trp Gln
Arg Arg Asp Thr Leu Ser Thr Ser Ser Leu Ser Gly Lys Gly Asn Phe Gly Ser

2511 2538
GCG TGG AGC TGT GCC GCT ATG ACC CCC TGG GGA CAA TAC GGG ACC CCT GGT GGC
Ala Trp Ser Cys Ala Ala MET Thr Pro Trp Gly Gln Tyr Gly Thr Pro Gly Gly
Arg Gly Ala Val Pro Leu . Pro Pro Gly Asp Asn Thr Gly Pro Leu Val Ala
Val Glu Leu Cys Arg Tyr Asp Pro Leu Gly Thr Ile Arg Asp Pro Trp Trp Gln

2565 2592
AGT GAA ACA GCT ACA GCA CAG CGT GCC AGA CCA GCA GAG GGA CTT CAG CGG GAG
Ser Glu Thr Ala Thr Ala Gln Arg Ala Arg Pro Ala Glu Gly Leu Gln Arg Glu
Val Lys Gln Leu Gln His Ser Val Pro Asp Gln Gln Arg Asp Phe Ser Gly Arg
. Asn Ser Tyr Ser Thr Ala Cys Gln Thr Ser Arg Gly Thr Ser Ala Gly Asp

2619 2646
ATT CAG ATC CTT AAG GCT CTG CAC AGC GAC TTC ATC GTC AAG TAC CGG GGA GTC
Ile Gln Ile Leu Lys Ala Leu His Ser Asp Phe Ile Val Lys Tyr Arg Gly Val
Phe Arg Ser Leu Arg Leu Cys Thr Ala Thr Ser Ser Ser Ser Thr Gly Glu Ser
Ser Asp Pro . Gly Ser Ala Gln Arg Leu His Arg Gln Val Pro Gly Ser Gln

1030 End Slow long

2673 2700
AGC TAT GGG CCA GGT CGC CAG AGC CTG CGT TGG TGA TGA GAT GCC GCA GGC GGC
Ser Tyr Gly Pro Gly Arg Gln Ser Leu Arg Trp . . Asp Ala Ala Gly Gly
Ala MET Gly Gln Val Ala Arg Ala Cys Val Gly Asp Glu MET Pro Gln Ala Ala

TTG GTG ATG GAG TAC TTG CCC AGC GGC

2727 2754

TTG CCT GCG AGA CTT CTG CAG [redacted] CAT CGC GGC CTG CAC ACC [redacted] CGC CTA CTG
Leu Pro Ala Arg Leu Leu Gln Arg His Arg Gly Leu His Thr Asp Arg Leu Leu
Cys Leu Arg Asp Phe Cys Ser Ala Ile Ala Ala Cys Thr Pro Thr Ala Tyr Cys
Ala Cys Glu Thr Ser Ala Ala Pro Ser Arg Pro Ala His Arg Pro Pro Thr Ala

2781 2808

CTG TTC GCT TGG CAG ATC TGC AAG GGC ATG GAG TAC CTG GGT GCG CGC CGC TGC
@eu Phe Ala Trp Gln Ile Cys Lys Gly MET Glu Tyr Leu Gly Ala Arg Arg Cys
Cys Ser Leu Gly Arg Ser Ala Arg Ala Trp Ser Thr Trp Val Arg Ala Ala Ala
Val Arg Leu Ala Asp Leu Gln Gly His Gly Val Pro Gly Cys Ala Pro Leu Arg

2835 2862

GTA CAC CGT GAC CTG GCT GCG CGC AAC ATC TTG GTG GAG AGC GAG GCT CAT GTG
Val His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val Glu Ser Glu Ala His Val
Tyr Thr Val Thr Trp Leu Arg Ala Thr Ser Trp Trp Arg Ala Arg Leu MET .
Thr Pro . Pro Gly Cys Ala Gln His Leu Gly Gly Glu Arg Gly Ser Cys Glu

2889 2916

AAG ATC GCG GAC TTC GGC CTC GCT AAG CTG CTG CCC CTG GGA AAG GAA CTA CTA
Lys Ile Ala Asp Phe Gly Leu Ala Lys Leu Leu Pro Leu Gly Lys Glu Leu Leu
Arg Ser Arg Thr Ser Ala Ser Leu Ser Cys Cys Pro Trp Glu Arg Asn Tyr Tyr
Asp Arg Gly Leu Arg Pro Arg . Ala Ala Ala Pro Gly Lys Gly Thr Thr Thr

2943 2970

CGT GGT CCG CGA GCC TGC CAA AGC CCC ATC TTT TGG TAT GCC CCG GAG TCC CTA
Arg Gly Pro Arg Ala Cys Gln Ser Pro Ile Phe Trp Tyr Ala Pro Glu Ser Leu
Val Val Arg Glu Pro Ala Lys Ala Pro Ser Phe Gly MET Pro Arg Ser Pro Tyr
Trp Ser Ala Ser Leu Pro Lys Pro His Leu Leu Val Cys Pro Gly Val Pro Ile

2997 3024

TCT GAC AAC ATC TTC TCC CGC CAA TCT GAC GTG TGG AGA GTT TCG GAG TGG TGT
Ser Asp Asn Ile Phe Ser Arg Gln Ser Asp Val Trp Arg Val Ser Glu Trp Cys
Leu Thr Thr Ser Ser Pro Ala Asn Leu Thr Cys Gly Glu Phe Arg Ser Gly Val
. Gln His Leu Leu Pro Pro Ile . Arg Val Glu Ser Phe Gly Val Val Leu

3051 3078

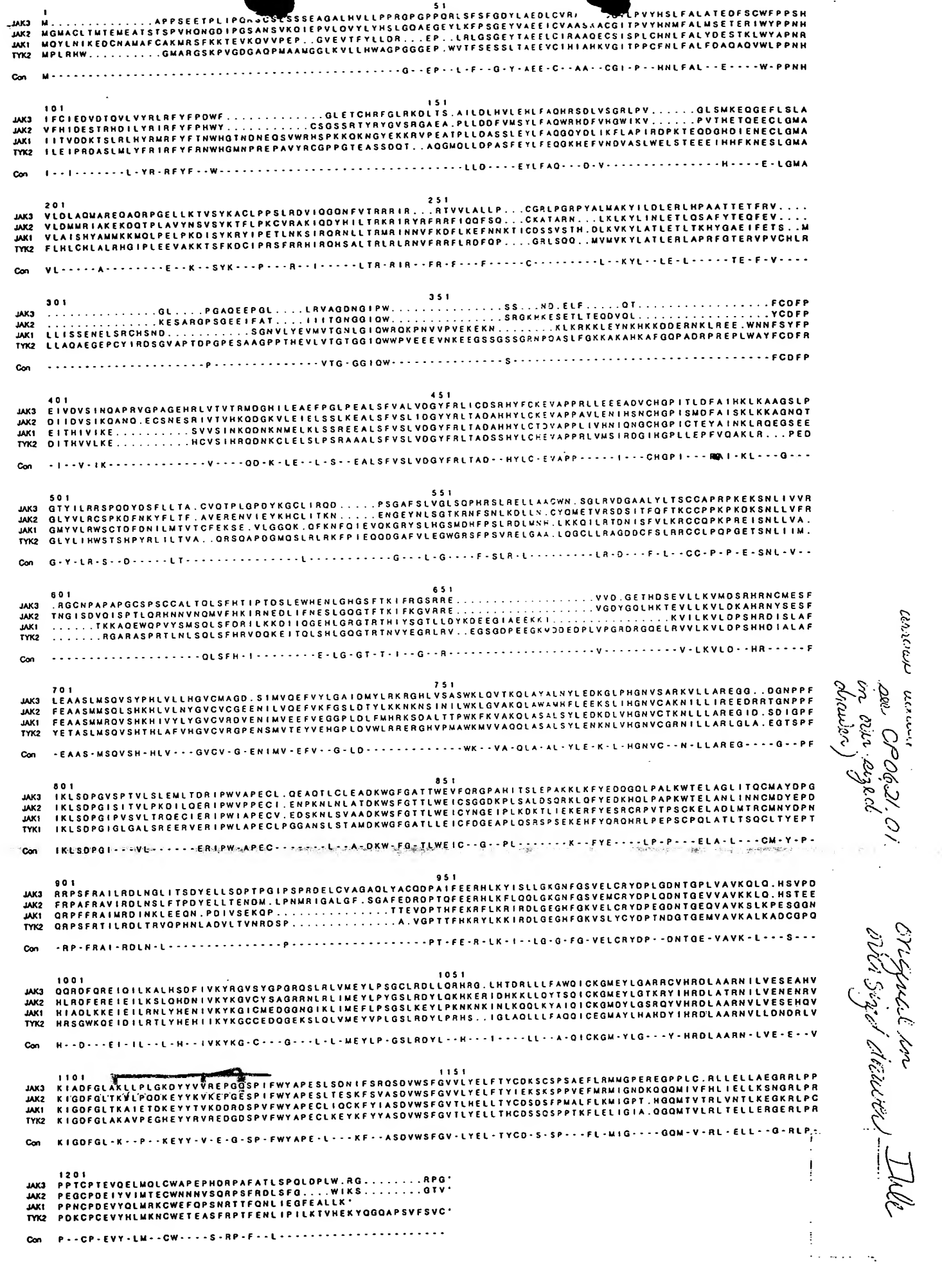
TGT ACG AGC TCN NNF NNN NNG CTC ATG CAG CTG TGC TGG GGC GTC CCA GCG CAC GCG CCC GAG CCG CAC
Cys Thr Ser Ser Leu MET Gln Leu Cys Trp Gly Val Pro Ala His
Val Arg Ala Ser Cys Ser Cys Ala Gly Ala Ser Gln Arg Thr
Tyr Glu Leu Ala His Ala Ala Val Leu Gly Arg Pro Ser Ala Arg

3105 3132

GAC CGG CCA GCC TTC GGA CCC TGA GCC CCC AGC TGG ACC CGC TGT GGC GTG GAA
Asp Arg Pro Ala Phe Gly Pro . Ala Pro Ser Trp Thr Arg Cys Gly Val Glu
Thr Gly Gln Pro Ser Asp Pro Glu Pro Pro Ala Gly Pro Ala Val Ala Trp Lys
Pro Ala Ser Leu Arg Thr Leu Ser Pro Gln Leu Asp Pro Leu Trp Arg Gly Arg

3159 3186

GAC CCC GGA TAG CAG CCA GGG GCG AGA GGG AGC TGC TGC AGT GGC TAG AGC AGA
Asp Pro Gly . Gln Pro Gly Ala Arg Gly Ser Cys Cys Ser Gly . Ser Arg
Thr Pro Asp Ser Ser Gln Gly Arg Glu Gly Ala Ala Ala Val Ala Arg Ala Glu
Pro Arg Ile Ala Ala Arg Gly Glu Arg Glu Leu Leu Gln Trp Leu Glu Gln Arg



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:
IHLE *et al.*
Appl. No. 08/665,574
Filed: June 18, 1996
For: **Jak Kinases and Regulation of Cytokine Signal Transduction**

Art Unit: 1819
Examiner: Hauda, K.
Atty. Docket: 0656.0370002/SLF/LBB

Declaration of Bruce A. Witthuhn and James N. Ihle Under 37 C.F.R. § 1.131

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

1. We, Bruce Witthuhn and James Ihle state that we are two of the named applicants of the above-captioned application and are co-inventors of the subject matter described and claimed therein.

2. Prior to April 1994, we and Dr. Ollie Silvennoinen reduced to practice in the U.S., the invention of the above-captioned application.

3. Said reduction to practice concerns at least those embodiments of the claimed invention that are related to DNA molecules comprising a DNA sequence encoding an amino acid sequence of a Jak3 kinase peptide and a vector or host comprising said DNA.

4. Prior to April 1994, two clones were obtained that were labeled as B1.1 and B3.1. *In vitro* translation experiments with T3 and T7 primers indicated that clone B3.1 was a partial clone and B1.1 was a full-length clone corresponding in length to other previously identified Jaks. *See* the third lane labeled as B1.1 T_3. **(Exhibit A)**

5. Following additional analysis completed prior to April 1994 it was established that the mJak3 expressed product could be competed out with a specific peptide to Jak3, thereby further supporting the assumption that a full length clone had been obtained. For example, *See* **Exhibit B**.

7. Upon information and belief, prior to April 1994, partial sequencing of subclones from B1.1 was completed by Dr. Silvennoinen. **(Exhibit C)**.

8. Following the partial sequencing of the B1.1 subclones, a full length mJak3 sequence of clone B1.1. was obtained prior to April, 1994. A working copy of this sequence is provided as **Exhibit D**.

9. Upon information and belief, prior to April 1994 a figure containing the complete amino acid sequence encoded by the full-length DNA of mJak3 was prepared by the Biomedical Communications Department at St. Jude. **(Exhibit E).**

10. All of the above results demonstrate that prior to April 1994, a full-length clone containing the mJak3 sequence had been obtained.

11. The attached are true and accurate photocopies (with dates blanked out) of pages taken from the notebooks or other sources of the inventors or those individuals supervised by the inventors.

12. We further state that all statements made are to our knowledge true and that all statements made on information and belief are believed to be true and further that willful false statements and the like are punishable by fine or imprisonment, or both under Section 1001 of Title 18 of the U.S. Code and may jeopardize the validity of the application or any patent issuing thereon.

Date

Bruce A. Witthuhn

FEB. 22, 1999

Date

James N. Ihle

FEB. 22, 1999

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

IHLE *et al.*

Serial No. 08/665,574

Filed: June 18, 1996

For: **Jak Kinases and Regulation of Cytokine Signal Transduction**

Art Unit: 1819

Examiner: K. Hauda

Atty Docket: 0656.0370002/SLF/LBB

Declaration Concerning Witthuhn *et al.*, "Involvement of the Jak-3 Janus Kinase in Signaling by Interleukins 2 and 4 in Lymphoid and Myeloid Cells." *Nature 30*:153-157, July 1994.

Honorable Commissioner of
Patents and Trademarks
Washington, DC 20231

Sir:

The undersigned, James N. Ihle, Bruce A. Witthuhn and Olli Silvennoinen each declare and state:

1. We are co-inventors of the subject matter described and claimed in the above-captioned patent application.

2. Each of us contributed to the conception of at least one pending claim in the invention of the above-captioned application.

3. We are also co-authors of the publication: Witthuhn *et al.* "Involvement of the Jak-3 Janus Kinase in Signaling by Interleukins 2 and 4 in Lymphoid and Myeloid Cells. *Nature 30*:153-157, July 1994.

4. The additional authors on the Witthuhn *et* al. publication (i.e. Osamu Miura, Koon Siew Lai, Christopher Cwik and Edison T. Liu) are not co-inventors and were either individuals working under the direction and/or supervision of at least one of the inventors of the above-referenced application or provided materials used in the publication.

5. The following co-authors of the publication contributed to said publication as follows:

a) Osamu Miura provided CTLL cells expressing the Epo receptor and was not involved in conception of the invention of the above-referenced application

b) Koon Siew Lai provided a PCR derived DNA fragment encoding a Jak and was not involved in conception of the invention of the above-referenced application.

c) Christopher Cwik provided technical support for the studies and was not involved in conception of the invention of the above-referenced application.

d) Edison T. Liu provided a PCR derived DNA fragment encoding a Jak and was not involved in conception of the invention of the above-referenced application

6. We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like

so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Respectfully submitted,

Dated:_____

James N. Ihle

Dated:_____

Bruce A. Witthuhn

Dated: May 20th, 1998

Ollie Silvennoinen

65603702.dec